TB for G/PHN Programs

Amy Bloom

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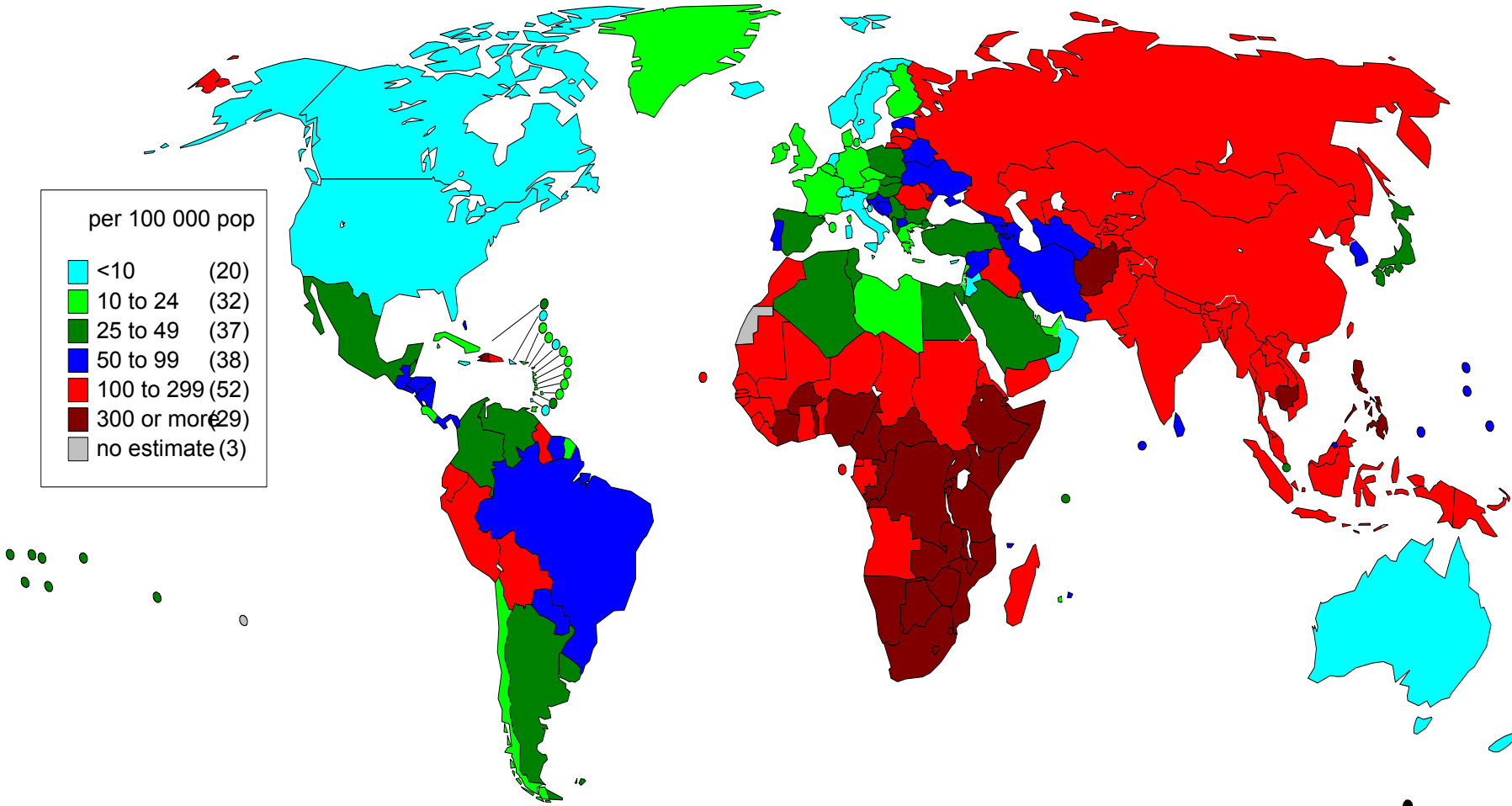
Setting the Stage

- TB kills 2-3 million each year: 5,000 a day, one every 10 seconds
- One third of the world's population is infected with TB; one person is newly infected every second
- As the HIV/AIDS epidemic escalates, so does the TB epidemic

Estimated TB Incidence



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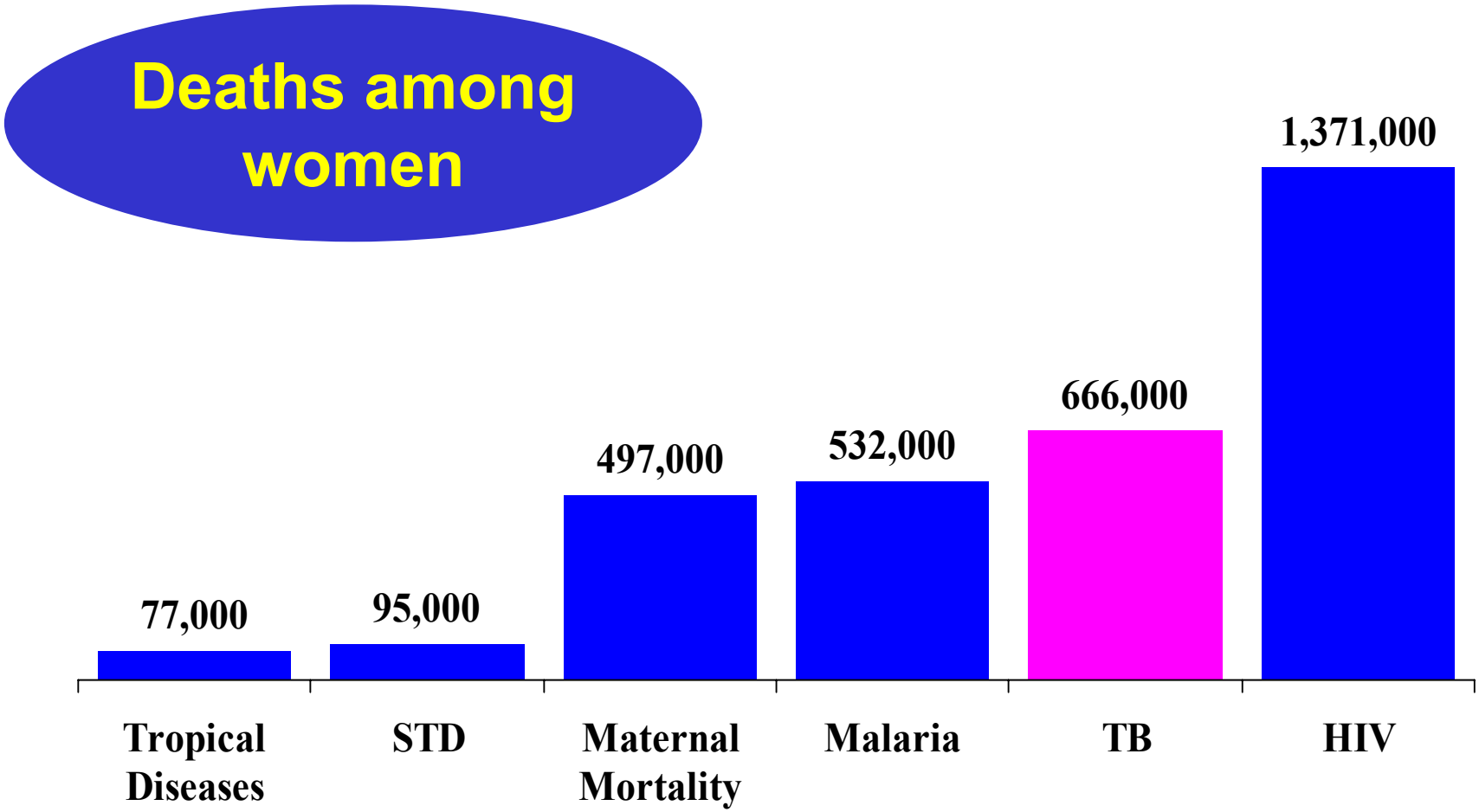
22 High Burden Countries

- India
- China
- Indonesia
- Nigeria
- Bangladesh
- Pakistan
- Philippines
- Ethiopia
- South Africa
- Russian Federation
- DR Congo
- Vietnam
- Kenya
- Brazil
- Tanzania
- Thailand
- Mozambique
- Myanmar
- Uganda
- Afghanistan
- Zimbabwe
- Cambodia

TB: A leading killer of women



Clinical Features

- TB is caused by Mycobacterium tuberculosis
- TB can affect any organ system: bone, kidney, CNS; 80% are pulmonary
- Active disease typical:
  - persistent cough > 3 weeks duration
  - +/-hemoptysis, decreased appetite, weight loss, general weakness, night sweats
- Treated for many years with long hospitalization, surgery, mult drugs, creating belief that TB incurable or that treatment is worse than disease

TB Infection vs TB Disease

- TB infection – organism is present, but dormant, cannot infect others
- TB disease – person is sick and can transmit disease to others if in lungs
- 10% of individuals with TB infection will develop TB disease, changes with HIV infection

TB Transmission

- Spread through the air
- Enters through the lungs
- Person with untreated pulmonary TB disease can infect 10-15 people each year

When Does TB Infection Become Disease?

- Most likely in first two years after infection
- If person becomes immunocompromised
  - HIV
  - Cancer
  - Chemotherapy
  - Poorly controlled diabetes
  - malnutrition

Priorities of TB Control

- Make sure the person completes TB treatment!
- Do not cause drug resistance; poor TB program worse than no TB program
- Treating non-pulmonary cases and those with infection, without active disease are of lesser public health importance

DOTS Strategy: 5 Essential Components

- Government commitment to an NTP
- Detection of infectious cases by sputum smear microscopy
- Standardized regimens of SCC, under direct observation for (at least) intensive phase
- Regular, uninterrupted supply of anti-TB meds
- Monitoring system for program supervision and evaluation

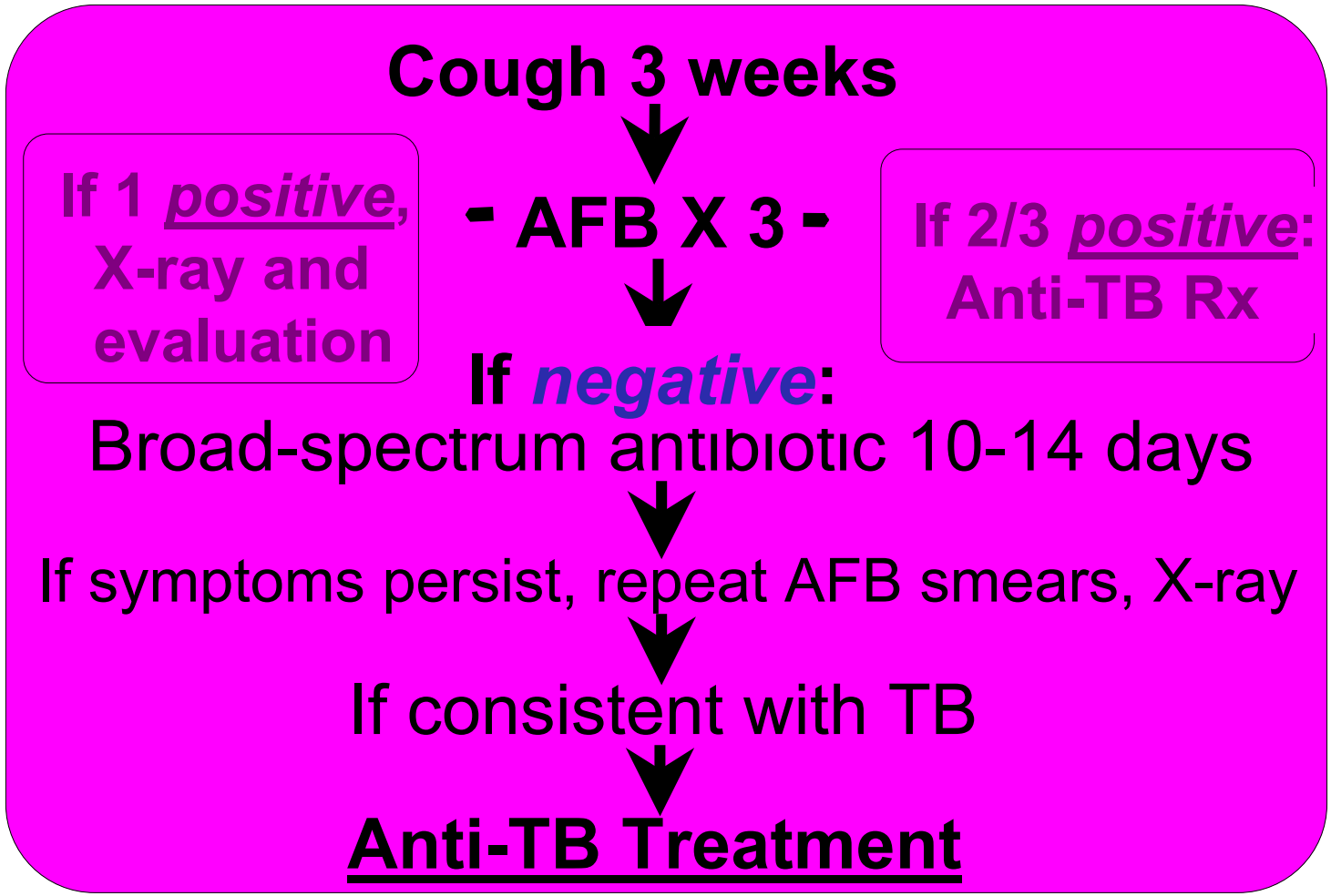
1. Political/Administrative Commitment

- Perception of TB as a priority problem with real solution
- Gov't acknowledges disease importance
- Public commitment to NTP
- Support for personnel, training, transport, drugs
- Advocacy to instill confidence that TB is curable and the epidemic controllable

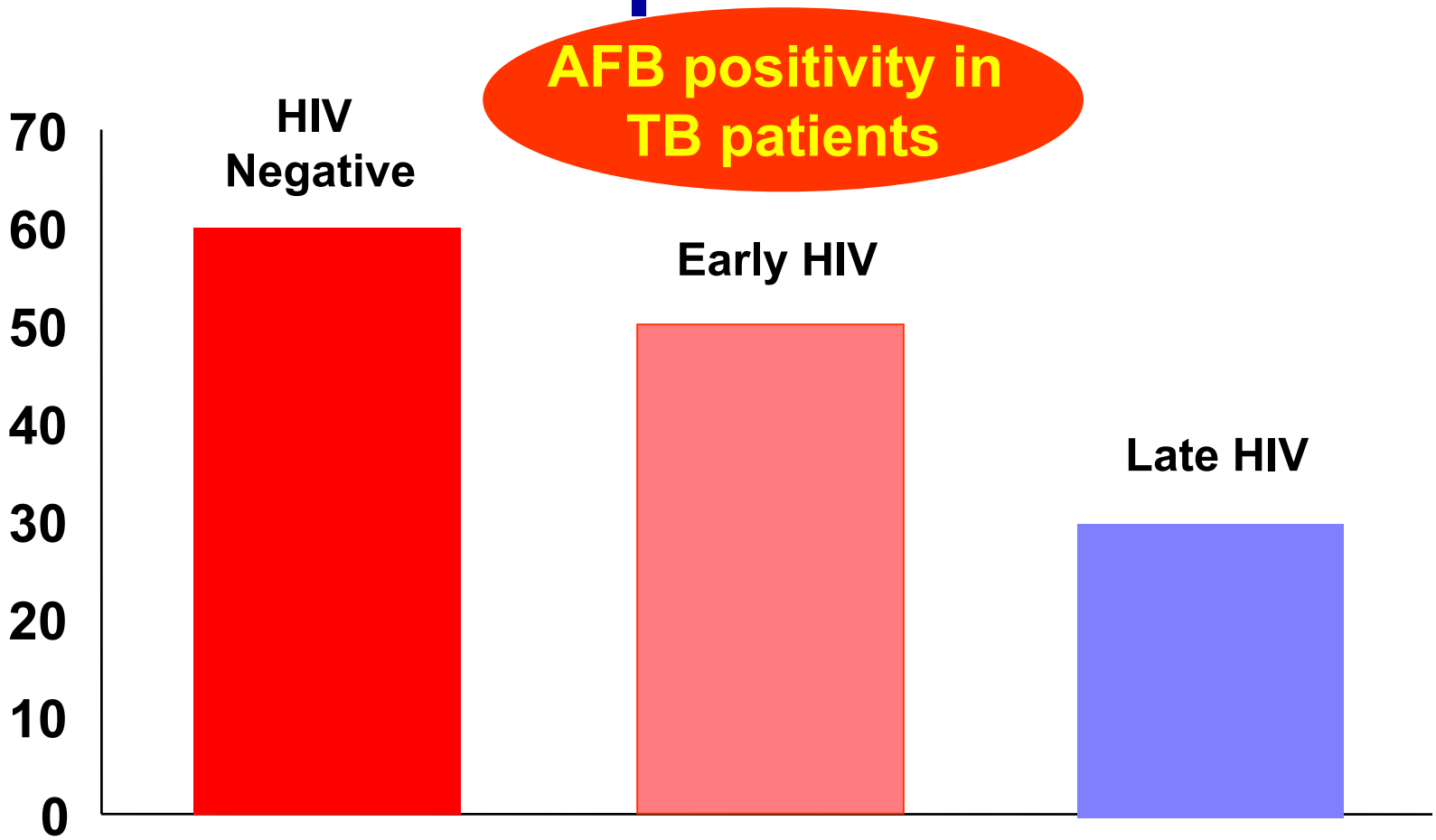
2. Accurate Diagnosis = Sputum Microscopy

- Identification/cure of infectious/smear + cases is highest priority of TB control
- Smear + patients are 4-20 times more infectious than smear-negative patients
- Untreated, smear + patients may infect 10-15 persons/year
- Smear + patients much more likely to die if untreated

Diagnosis of Pulmonary TB



Proportion of AFB + pulmonary TB patients



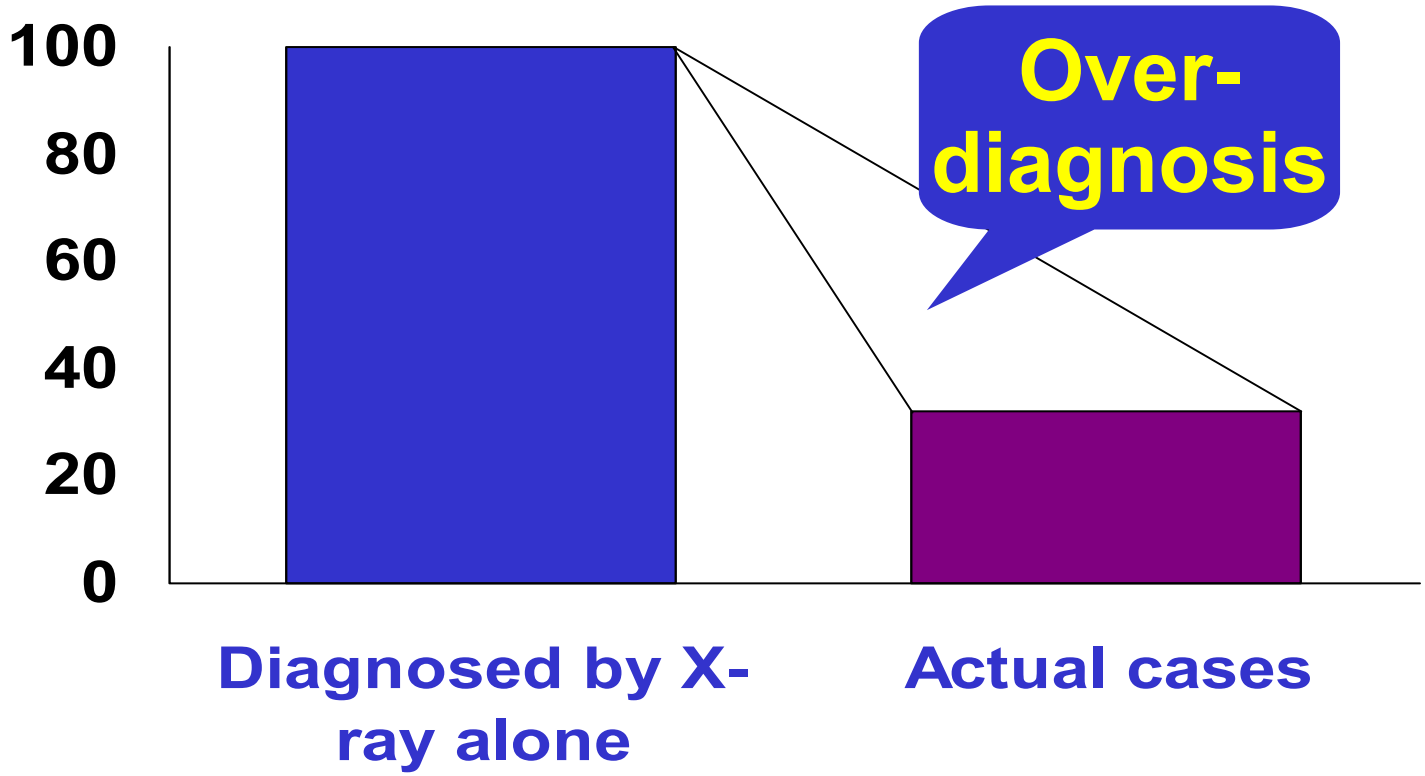
Chest XR As Diagnostic Tool

- No chest X-ray pattern absolutely typical
- 10-15% of culture-positive TB patients not diagnosed as TB by X-ray
- 40% of patients diagnosed as having TB on the basis of x-ray alone do not have active TB

$\Rightarrow$ X-ray is unreliable for diagnosing and monitoring treatment of tuberculosis

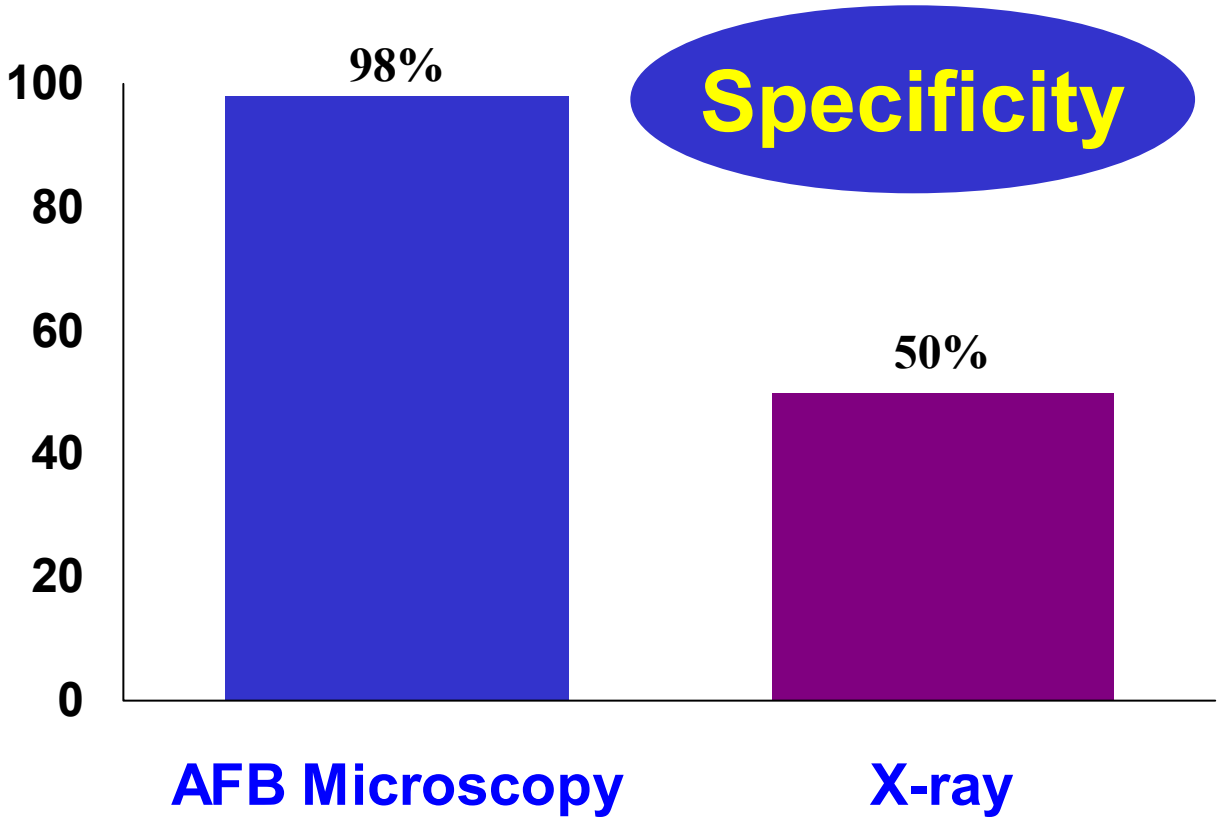
Toman K. Tuberculosis case finding and chemotherapy. WHO, 1979

XR-based Evaluation of TB



NTI, Ind J Tuberc, 1974

Microscopy more specific than XR for TB diagnosis



3. Adequate Supply of Drugs

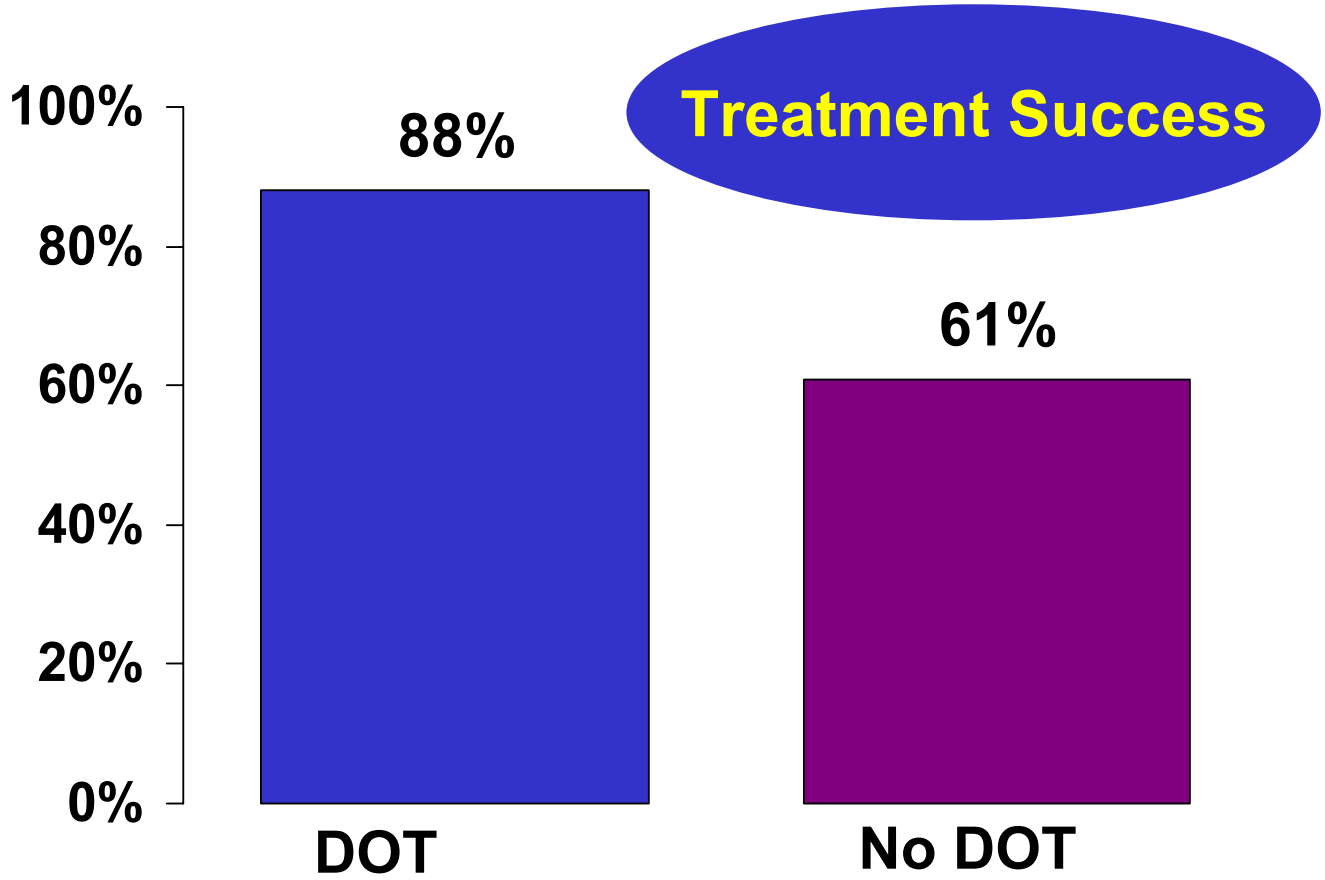
- Treatment: regular doses of combination regimens for >6 months
- Identification of adequate supply of appropriate drugs prior to treatment initiation
- Incomplete rx leads to drug-resistant strains which are hard or impossible to cure
- Requires continuum of drug mgt services: selection, procurement, distribution, use.

4. Directly Observed Treatment

- Why? Many pts don't take medicines regularly, even if excellent health education provided
- Who? All pts... impossible to predict which patient will take medicine (1/3 not adherent)
- What? Observer watches and helps patient swallow tablets
- Where? Anywhere! (home, clinic, work, school, etc)
- Who does it? HCW, community liaisons, teachers,

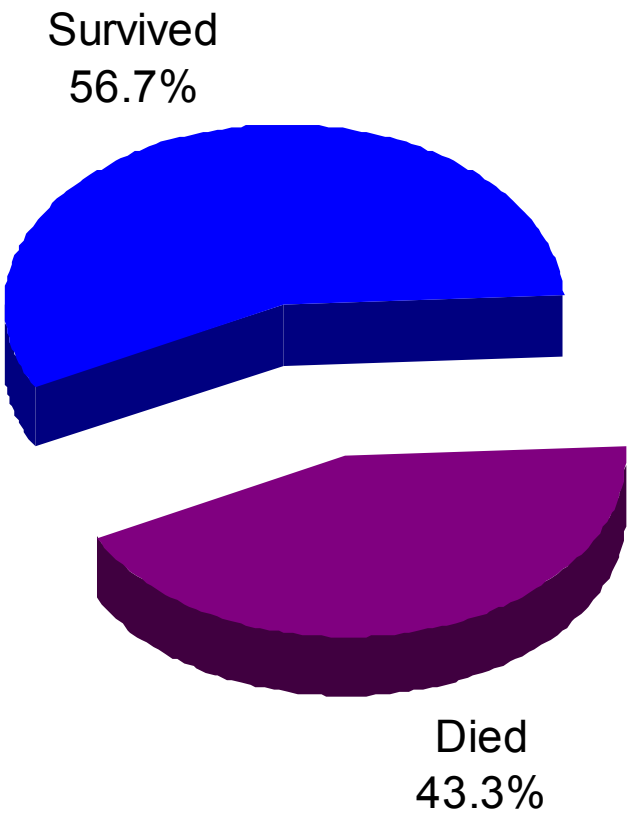
Direct observation ensures treatment for entire course with the right drugs, in the right doses, at the right intervals

DOT necessary even when drug supply ensured

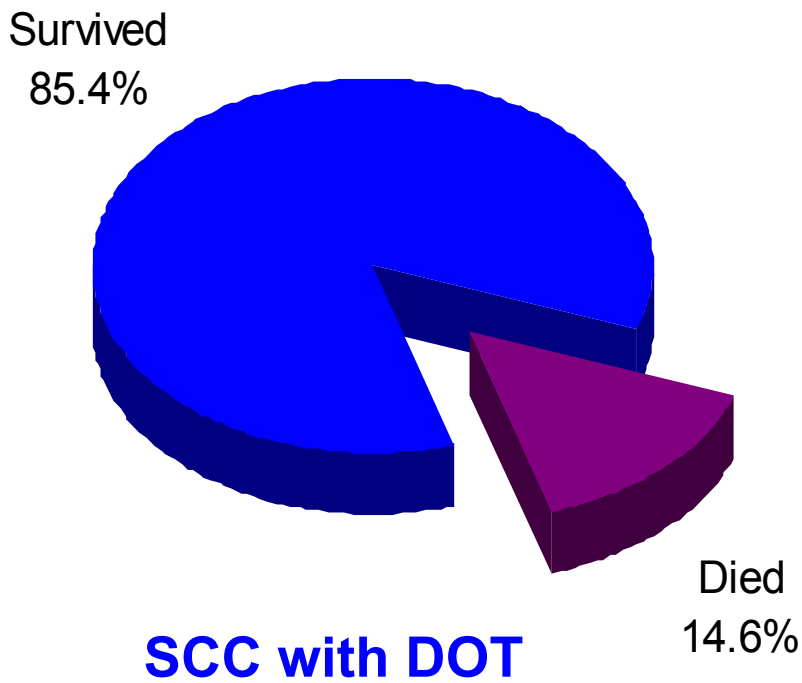


Chaulk CP. JAMA 1998;279:943-8

DOT prolongs survival of HIV-infected TB patients



SCC without DOT



SCC with DOT

5. Systematic Monitoring/Accountability

- Recording system simple to use, integrated component of DOTS enabling:
  - Monitoring of patient outcomes
  - Evaluation of program performance
  - Analysis of epidemiologic data
  - Identification of areas for OR
- Every level of health system accountable for patient diagnosis and cure; “report card”

Role of Rifampicin

- Necessary for short-course treatment
- Essential for at least first 2 months
- Bactericidal for rapidly dividing and slow-growing organisms
- Prevents emergence of resistance to other drugs
- Intermittent rx more effective than daily rx in animal model; equally effective in clinical trials

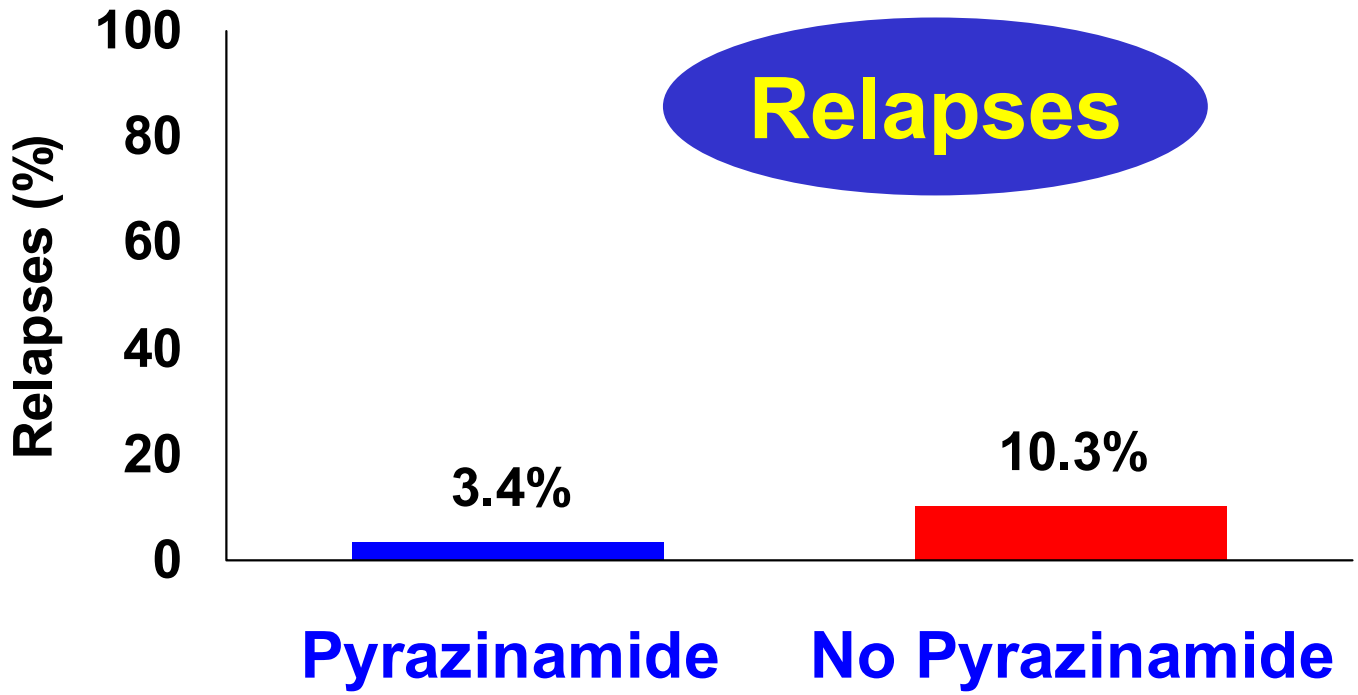
Role of Isoniazid

- Mainstay of anti-TB treatment
- Life saving in TB meningitis
- Bactericidal for rapidly dividing organisms
- Prevents emergence of resistance to other drugs
- Intermittent rx more effective than daily rx in animal model; equally effective in clinical trials
- Safe and effective for preventive treatment

Role of Pyrazinamide

- Essential for 6- and 8-month regimens
- No benefit if given > 2 months
- Relatively ineffective at preventing emergence of resistance to other drugs

Pyrazinamide essential for first two months of 6/8-month treatment



Am Rev Respir Dis 1987;136:1339-42

Role of Ethambutol/ Streptomycin

- Prevent emergence of resistance to other drugs given
- Hasten sputum conversion
- Bacteriostatic or weakly bactericidal against rapidly dividing organisms

Adverse reactions to anti-TB drugs

Drugs	Adverse reactions
Isoniazid	● Peripheral neuropathy ● Hepatitis
Rifampicin	● Gastroentestinal (anorexia, nausea, vomiting, abdominal pain) ● Hepatitis ● Reduced effectiveness of oral contraceptive pill
Pyrazinamide	● Joint pains ● Hepatitis
Ethambutol	● Optic neuritis
Streptomycin	● Auditory &vestibular nerve damage (also tofoetus) ● Renal damage

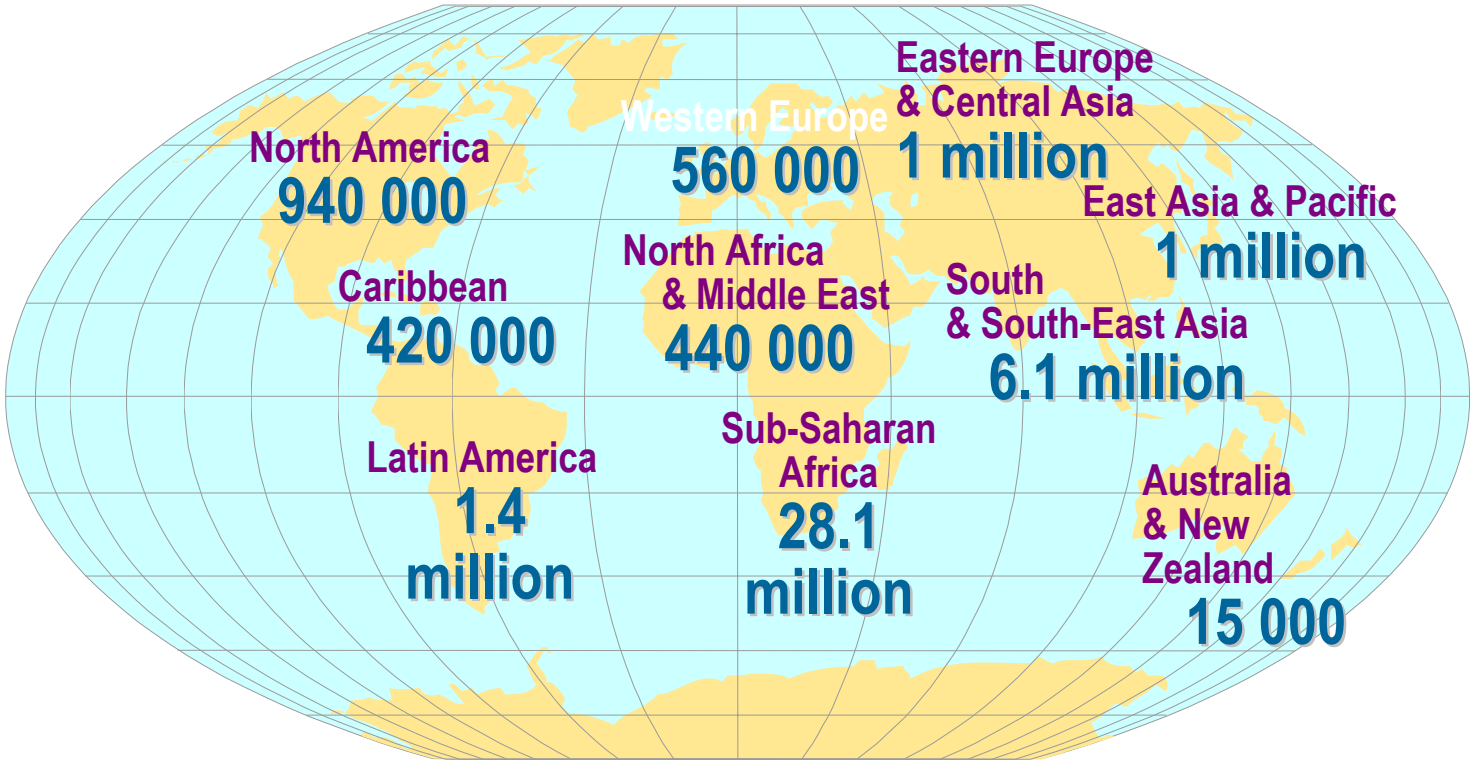
Multidrug-Resistant TB (MDRTB)

- Poorly supervised, incomplete treatment of TB worse than no treatment
- MDRTB is caused by inconsistent or partial treatment of susceptible TB (primary)
- Cure rates <70% cause the TB epidemic and drug resistance to increase
- MDRTB is more difficult/expensive to treat, and more likely fatal in developing world

TB and HIV/AIDS

- HIV and TB increase other's progression
- HIV+ individuals infected with TB are 30x more likely to develop TB disease
- TB is leading cause of death among HIV+
- TB accounts for 30-40% of AIDS deaths in Africa and Asia

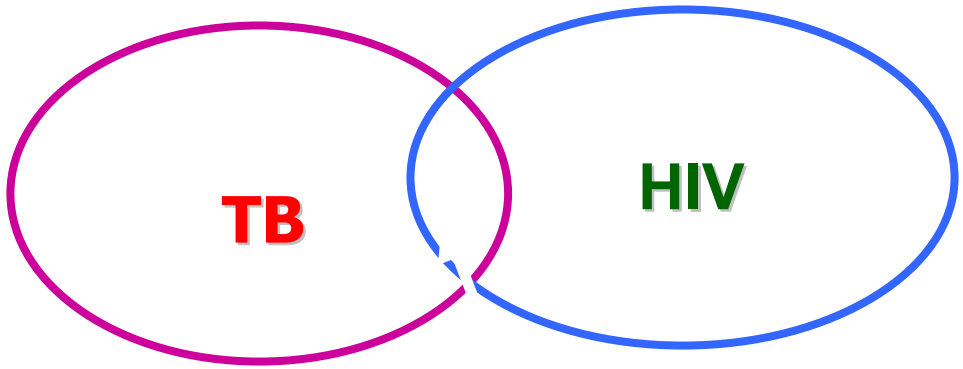
Adults and children estimated living with HIV/AIDS at end 2002



Total: 43 million

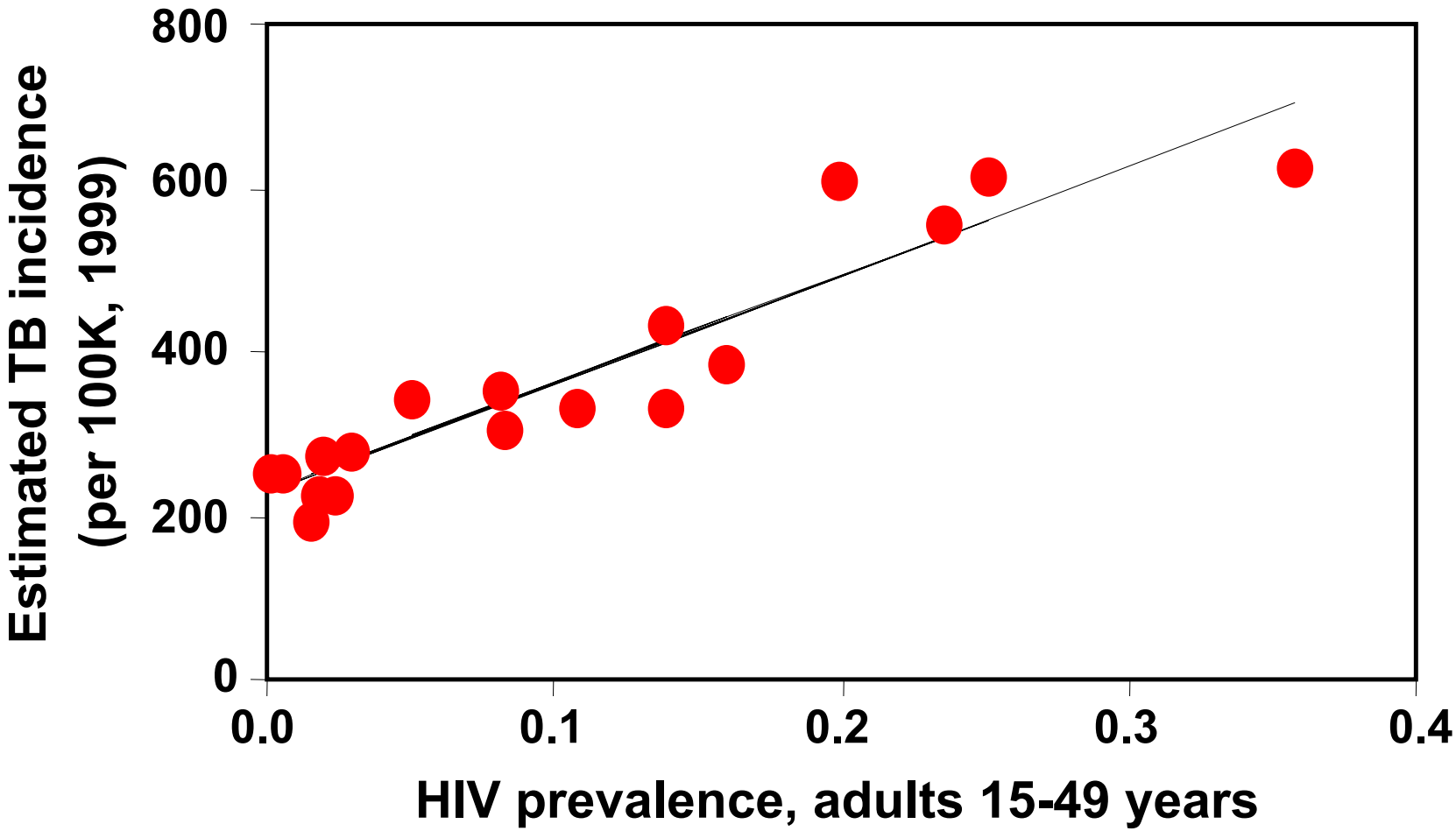
TB-HIV overlapping epidemics

The impact of HIV on the TB epidemic depends on the size of the overlap between the TB-infected and HIV-infected populations



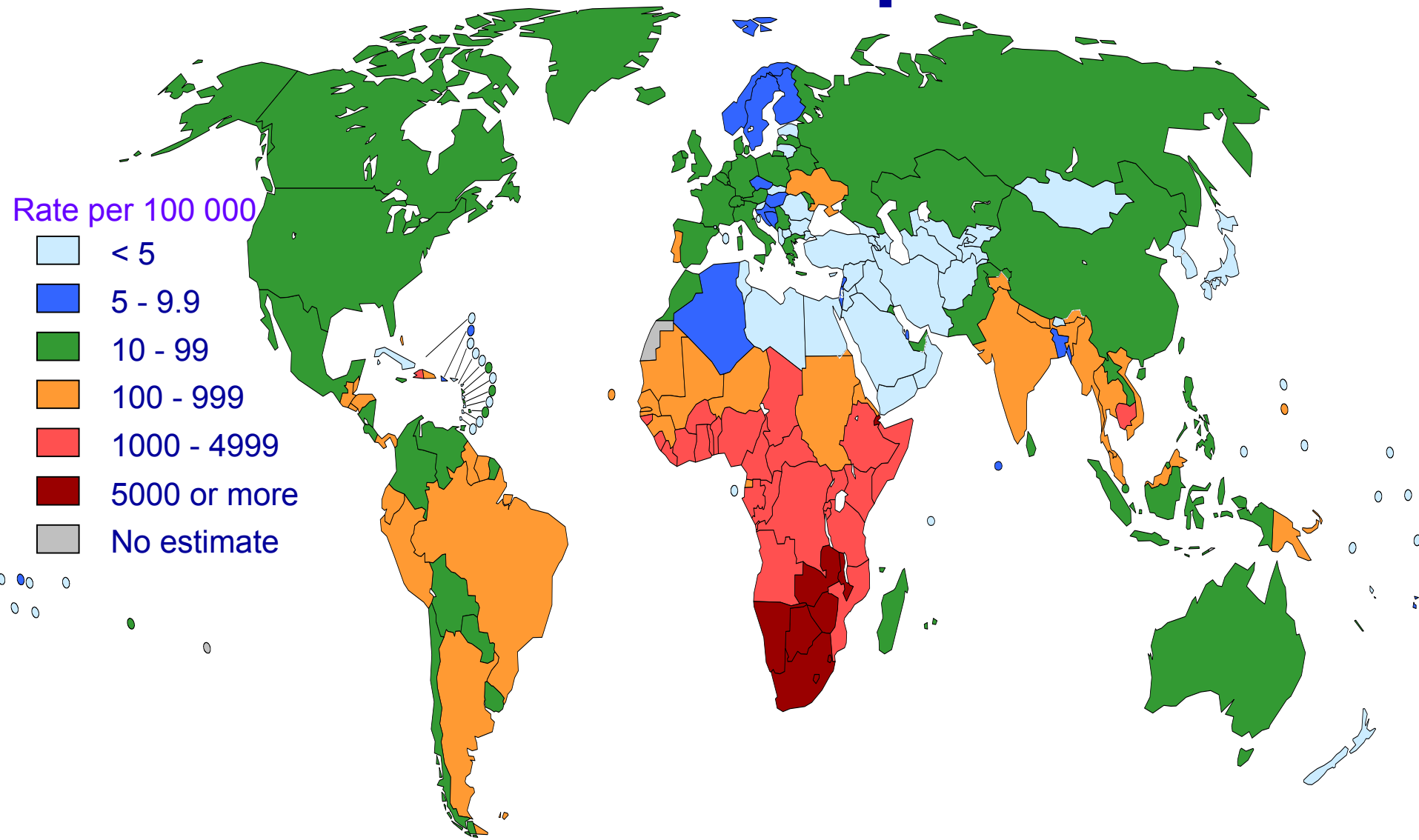
TB and HIV

TB incidence vs HIV prevalence



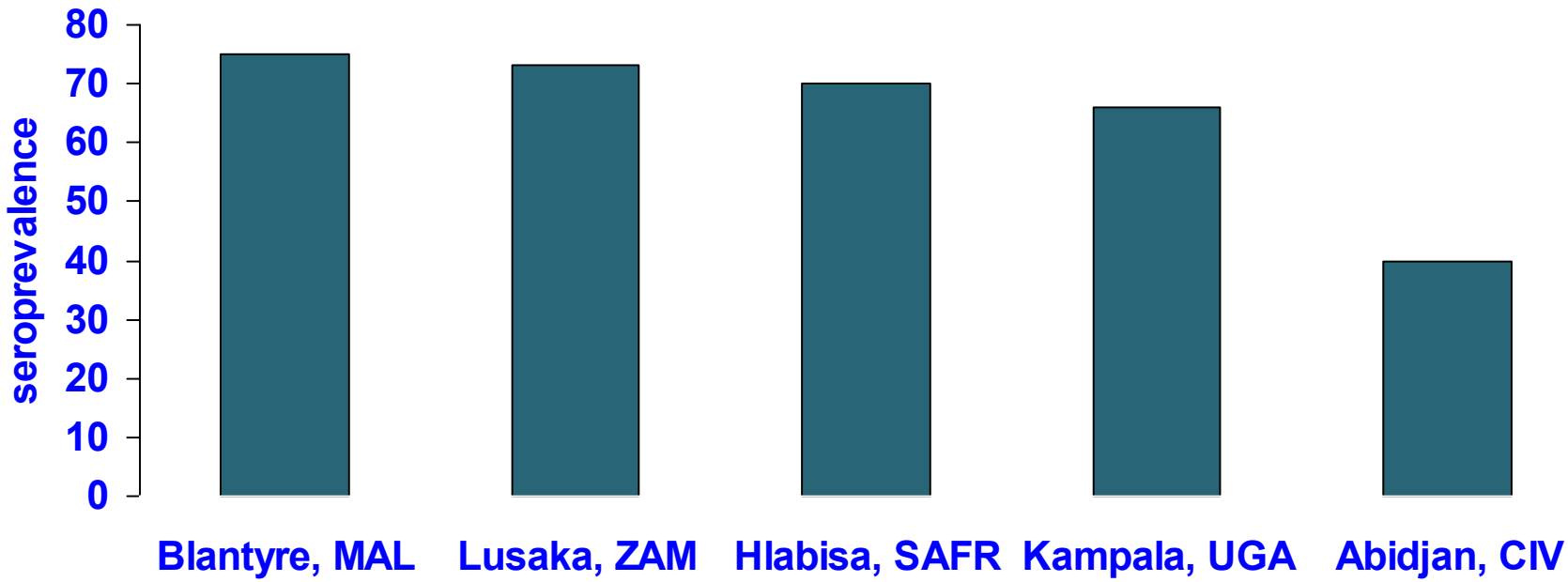
Source: Dye C et al, JAMA 1999

Est TB-HIV co-infx prevalence



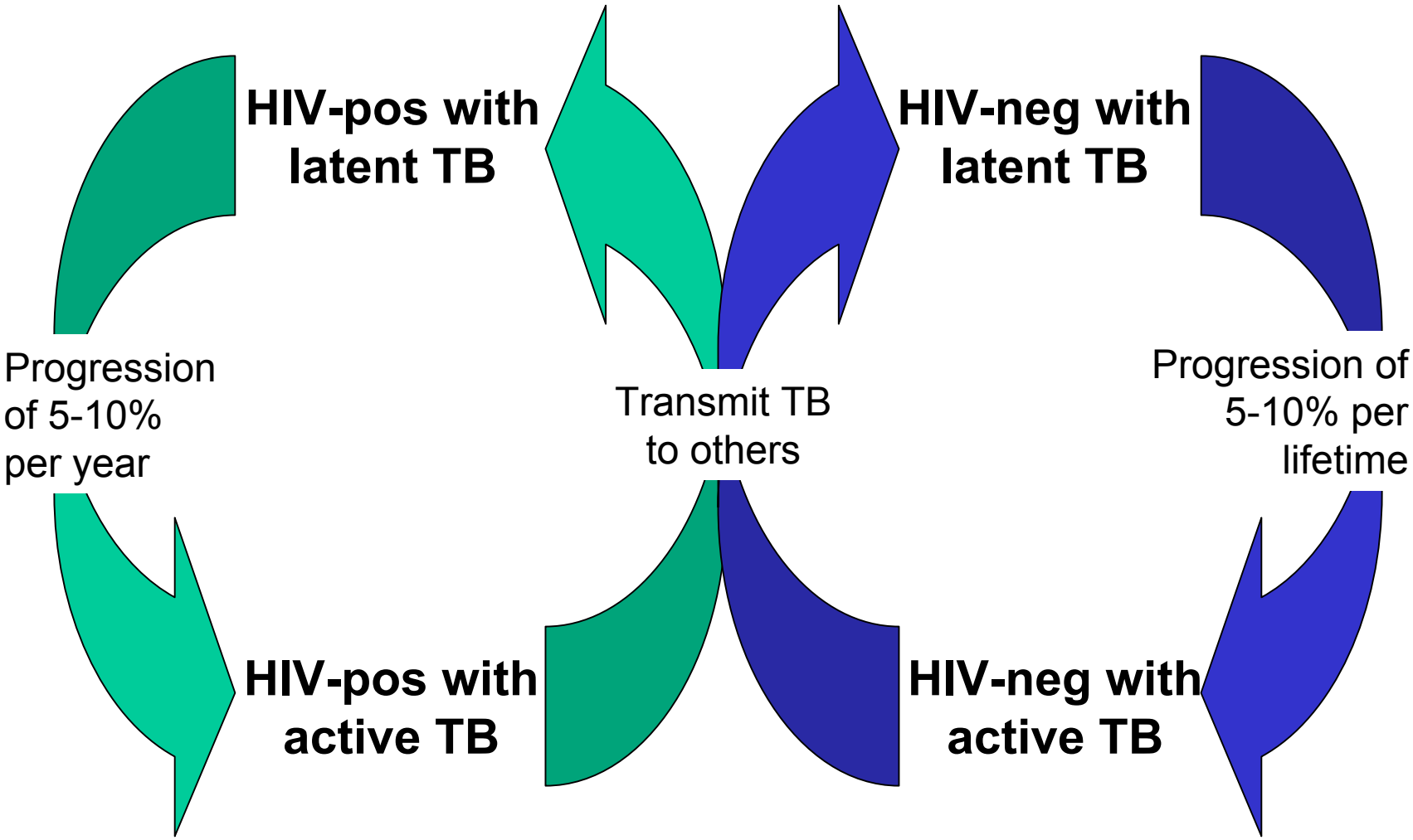
Source: Corbett EL, Watt CJ, Walker N, Maher D, Raviglione MC, Williams B, Dye C. (Arch Int Med in press)

HIV seroprevalence in TB cases Africa, 1988-1997



Why highlight HIV/AIDS?

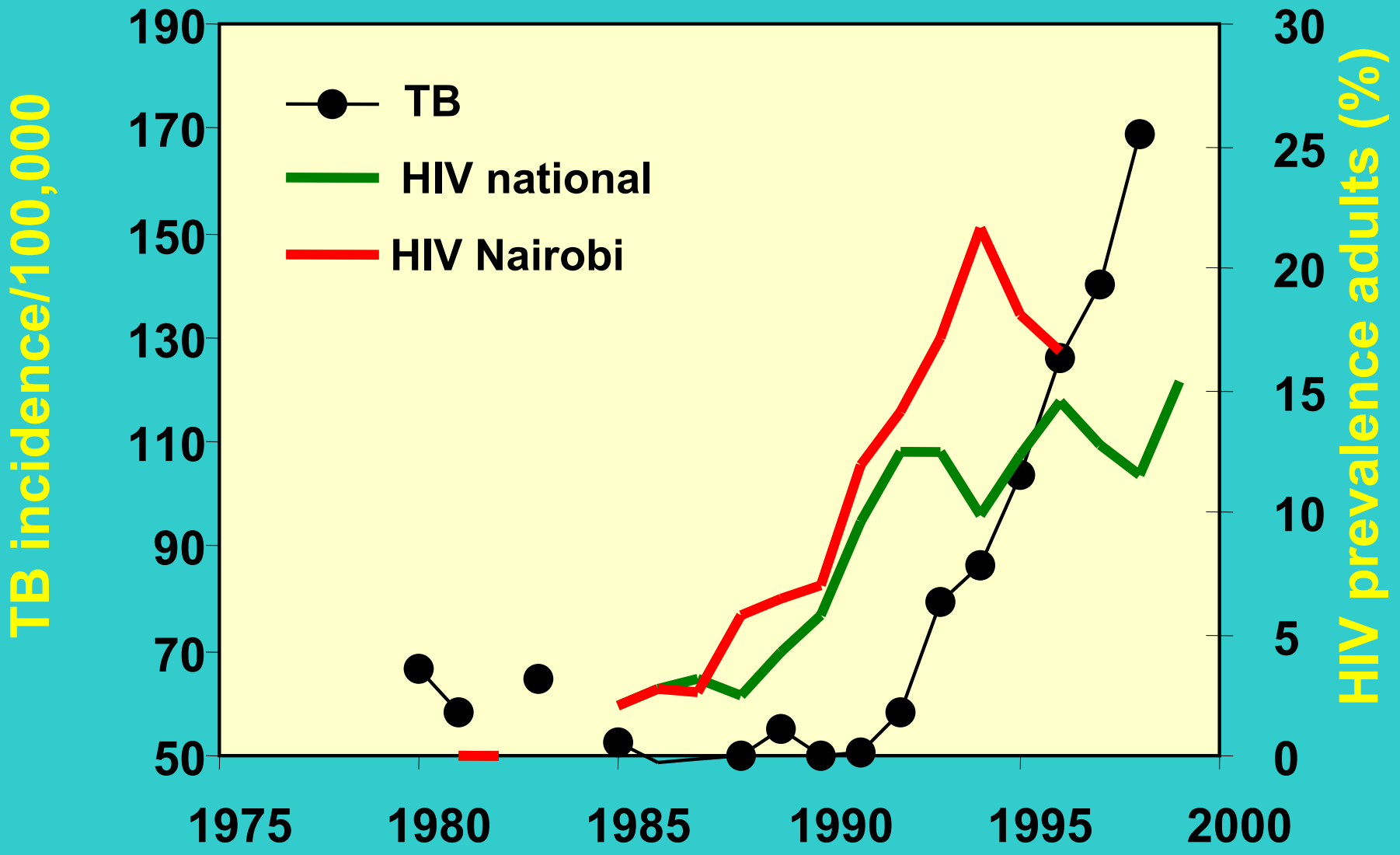
- Most potent risk factor ever identified for converting latent TB to active TB
- Most potent risk factor for death (aside from no treatment) among TB patients -- 1/3 die during treatment
- In communities with high prevalence of HIV/TB co-infection
  - Greatly increased TB morbidity and mortality
  - Health services overwhelmed


HIV-pos with latent TB
HIV-neg with latent TB
Progression of 5-10% per year
Transmit TB to others
Progression of 5-10% per lifetime
HIV-pos with active TB
HIV-neg with active TB

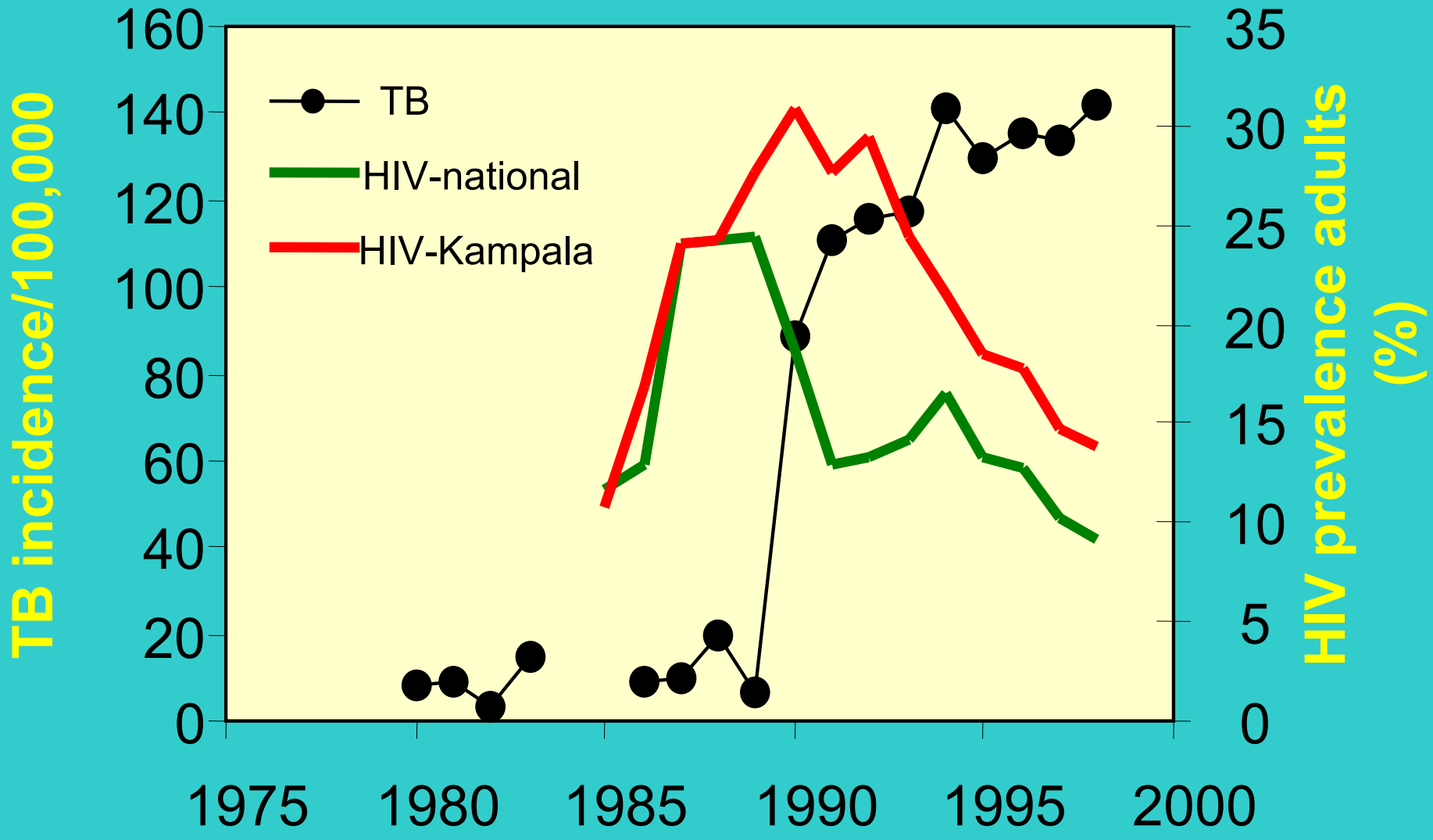
Diagnosis of HIV-Related TB

- Sputum smear sensitivity reduced in HIV-related TB (20-30% lower)
- Extrapulmonary TB more common (30-50% of cases)
- Need for culture and biopsy
- Presumptive therapy

Dynamics of TB and HIV in Kenya



Dynamics of TB and HIV in Uganda



TB Incidence and HIV Prevalence, Botswana

Failure of "Successful" DOTS Program to Control TB

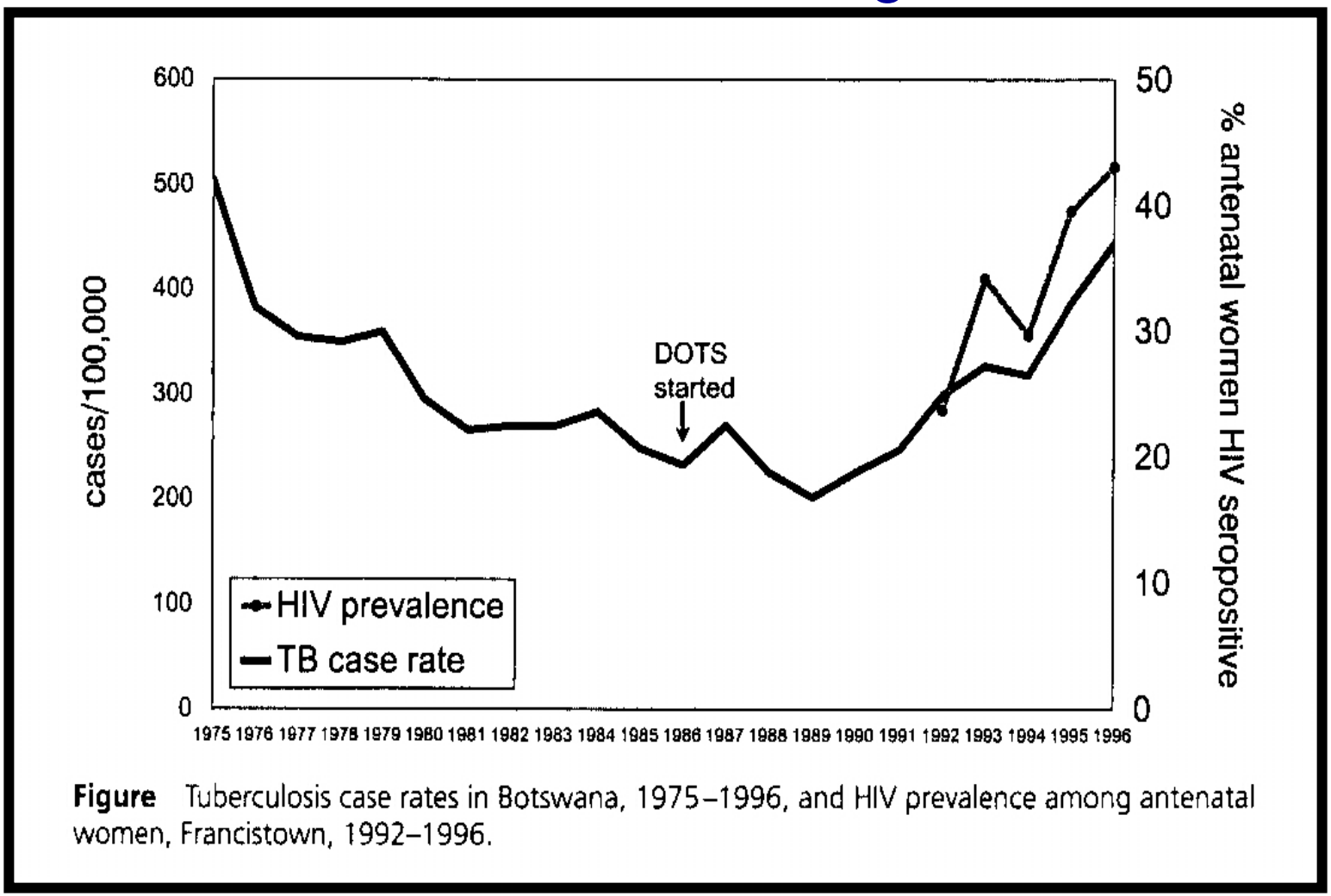


Figure Tuberculosis case rates in Botswana, 1975–1996, and HIV prevalence among antenatal women, Francistown, 1992–1996.

Kenyon et al., Int J TB Lung Dis 1999;3:4-11

Framework for TB-HIV Program

For National AIDS & National TB Control Programs:

- Each should have clearly defined responsibilities
- Interventions for TB-HIV in each program should be complementary
- Joint responsibility for surveillance of TB-HIV

Imperatives to Controlling HIV-Related TB

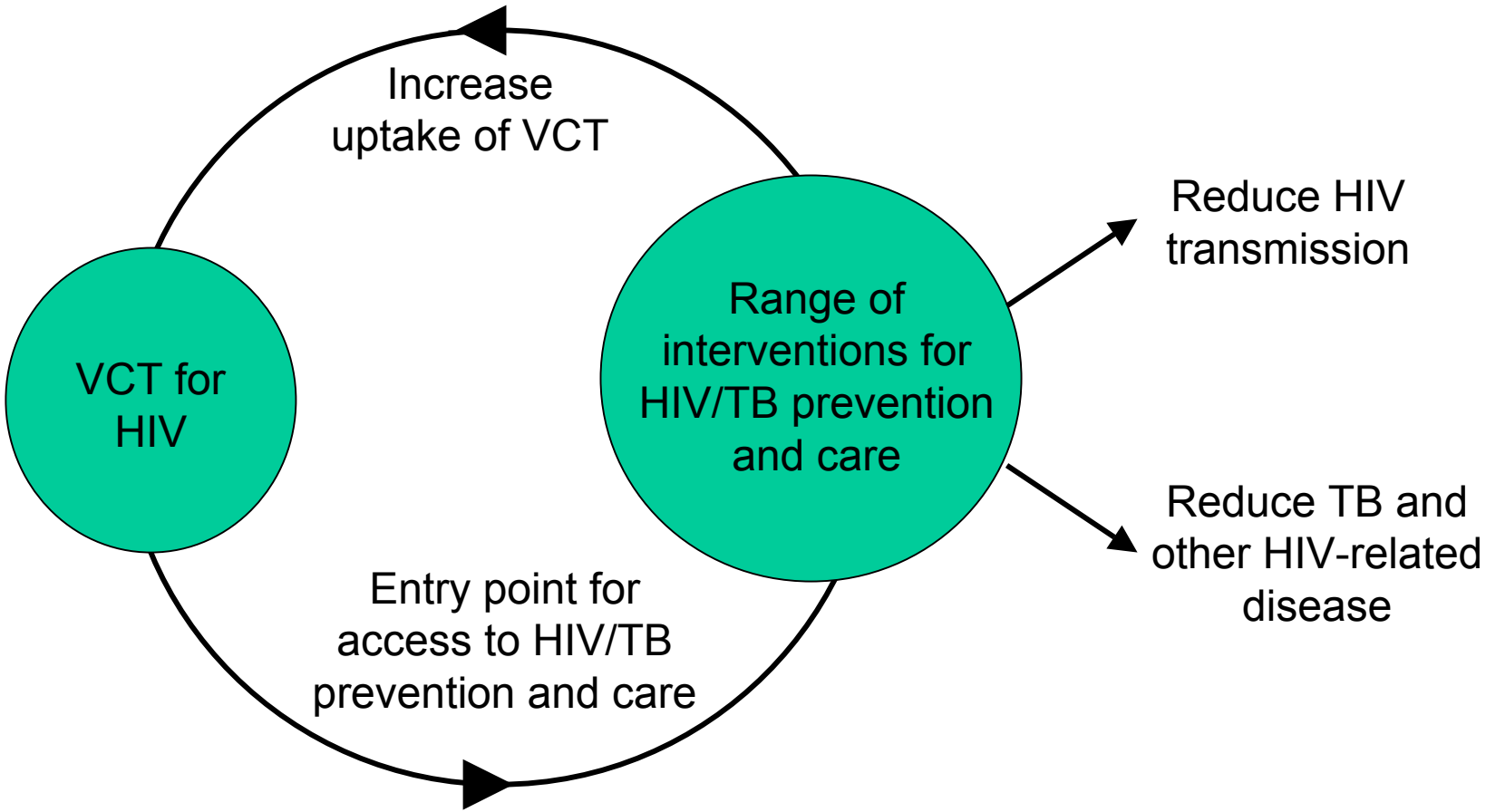
- Expand and strengthen DOTS
- Increase detection (active case finding)
- HIV counseling and testing

- Treatment of HIV+ patients with latent TB
- Use of HAART, where appropriate
- Develop effective HIV *and* TB vaccines

International Approach to TB/HIV Co-epidemic

- Evolving over time
- Development of district-based model for the integrated delivery of TB and HIV services
- ProTEST projects – linking voluntary counseling and testing to TB/HIV prevention and care
- Multiple pilot sites: Malawi, South Africa, Zambia, Uganda since 1999; newer sites in Asia

TB and HIV Partnerships



Anti-retroviral therapy

- Highly active antiretroviral therapy (HAART) reduces risk for developing active TB
- Substantial pressure on governments and IOs to utilize HAART
- Need for more OR on feasibility of HAART, delivery models in developing countries, and impact on TB

HAART for co-infected in developed countries: advantages

- HAART reduces risk of TB by >80%
- HAART patients had fewer new AIDS-illnesses
- INH prev therapy may prolong survival, even in those with access to HAART
- Current rec: Start HAART if CD4 <100, otherwise defer

HAART for co-infected in dev countries: disadvantages

- Lack of health system preparedness
- Patients on HAART still have a risk of developing TB
- 34% of pts had TB or HIV regimen changed due to adverse reactions
- HAART guidelines for developing countries miss large proportion of those who will develop TB (DC4>200)
- High cost

Summary

- 1/3 of the world is infected with TB
- Treatment of active TB is critical to prevention of new cases of TB
- DOTS needs to be expanded and strengthened to decrease morb/mort of TB, prevent MDRTB, and curb HIV/TB
- 1/3 of those with HIV will develop TB
- TB is a key part of HIV/AIDS care
- Prevention of HIV is crucial to control TB

Essential Concepts for TB Programs/Integration

- Access is necessary but NOT sufficient
  - Drugs
  - Services
- Not every health center/NGO or PHN site appropriate as TB care center
- “Something/anything is better than nothing” does not apply here!

Essential Concepts for TB Programs/integration

- Demand for services should NEVER be created before services available
- Community approaches to care seeking, KAP essential for providers/pts
- Key to examine/reorganize services to avoid missed opportunities
- Alternatives to HCW providing DOT
- TB is still stigmatized!!

Priorities of TB Control

- Make sure the person completes TB treatment!
- Don’t create drug resistance; a poor TB program is worse than no TB program!
- Treating non-pulmonary cases and those infected without active disease of lesser public health importance

With TB, Treatment Is More Than Treatment, Treatment Is Prevention